# Statistical Analysis of the Diagnostic Accuracy of Morphological Features in the Cytological Diagnosis of Proliferative Breast Lesions

## Fine Needle Aspiration Compared to Histological Diagnosis

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## Certificate of Authorship

I certify that the substance of this thesis has not been submitted already for any degree and is not being submitted currently for any other degree.

I certify that any help received in preparing this thesis, and all sources used, have been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

Signature of Candidate

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## List of Abbreviations for Non-cytological Criteria

| | |
|---|---|
| aden | adenosis |
| ADH | atypical ductal hyperplasia |
| ALH | atypical lobular hyperplasia |
| Ca | carcinoma |
| CIPL | complex intraduct papillary lesion |
| col cell hyperpl | columnar cell hyperplasia |
| CSL | complex sclerosing lesion |
| DCIS | ductal carcinoma *in situ* |
| DD | differential diagnosis |
| EH | epithelial hyperplasia |
| EHA | epithelial hyperplasia with atypia |
| FA | fibroadenoma |
| FCC | fibrocystic change |
| FHWA | florid epithelial hyperplasia with atypia |
| FNAB | fine needle aspiration biopsy |
| intra comp | intraduct component |
| L | left/lower |
| LCIS | lobular carcinoma *in situ* |
| LG | low grade |
| ND | not diagnostic of a specific lesion |
| NEOM | no evidence of malignancy |
| NI | not indicated |
| NOS | not otherwise specified |
| O | outer |
| pap Ca | papillary carcinoma |
| pap | papilloma |
| PBL | proliferative breast lesion |
| PL | papillary lesion |
| PPV | positive predictive value |

**List of Abbreviations for Non-cytological Criteria (continued)**

| | |
|---|---|
| PSB | proteinaceous material |
| Q | quadrant |
| R | right |
| RS | radial scar |
| SBC | Sydney Breast Clinic |
| scler | sclerosing |
| SF | stromal fragment |
| TC | tubular carcinoma |
| TF | tissue fragment |
| U | upper |

## List of Abbreviations for the Cytological Criteria

| | |
|---|---|
| aniso | nuclear size variation |
| antler | antler horn, drumstick tissue fragments |
| apo sheet | apocrine sheets |
| atyp disp | dispersed atypical cells |
| BBN | bare bipolar nuclei |
| Ca2+ epith | psammomatous calcifications – in epithelium |
| Ca2+ in pap | psammomatous calcifications in papillary fragments |
| Ca2+ stroma | psammomatous calcifications – in stroma |
| chromatin | nuclear pleomorphism of chromatin |
| cohesion | cohesion vs discohesion |
| coll spher | collagenous spherulosis |
| comp EH | cohesive tissue fragments folded, mildly complex, branched with myoepithelial cells; may show some apocrine differentiation |
| disorg frond | more complex papillae with thin disorganized fronds |
| disp + TF | largely dispersed cells with scattered small or large tissue fragments |
| disp apo | dispersed apocrine cells |
| disp epith | dispersed epithelial cells |
| dispersed | dispersed cells with a few small discohesive tissue fragments of 5-20 cells |
| FA stroma | rounded, club ended, "clover leaf", smooth edged – "fibroadenoma" stroma |
| free Ca2+ | psammomatous calcifications – free |
| free gran | granular calcifications – free |
| hard-edge | three dimensional, round, hard-edged, branched tissue fragments |
| hypercell | hypercellular (" cellular fibroadenoma") stroma |
| hyperchrom | nuclear hyperchromasia |
| L+S | large tissue fragments with scattered small tissue fragments with bare bipolar nuclei and few dispersed cells |
| large ball | large rounded, balled up, isolated tissue fragments |
| large nucleo | single and large nucleoli |

## List of Abbreviations for the Cytological Criteria (continued)

| | |
|---|---|
| large TF | large tissue fragments with bare bipolar nuclei and few dispersed cells |
| long strip | columnar cells in long strips/palisading arrays (>6 cells) |
| MEC | myoepithelial cells within tissue fragments |
| meshwork | "meshwork" – thin stroma surrounding tubules/acini/epithelial clumps/nests |
| mitosis | mitoses |
| mix | mix of large and small tissue fragments with bare bipolar nuclei and some dispersed cells |
| multi nucleo | multiple nucleoli |
| myxoid | myxoid stromal fragments typical of FA |
| naked aty | stripped, enlarged atypical nuclei |
| necrosis | granular necrosis |
| normal st | unremarkable stromal fragments with some spindly nuclei |
| nuclei enlarge | nuclear enlargement |
| old bl/sid | old blood with or without siderophages |
| pap large tip | papillae – micropapillary with no visible fibrovascular core (tips larger than base) |
| pap w FVC | papillae – with visible fibrovascular core (papillary fragments) |
| pap wo FVC | papillae – three dimensional structure with no visible fibrovascular core |
| PSB | proteinaceous material without cells |
| PSB/mos | proteinaceous material with foamy macrophages |
| PSB/mos/sid | proteinaceous material with foamy macrophages and siderophages |
| PSB/sid | proteinaceous material with siderophages |
| ragged dis | ragged, discohesive tissue fragments |
| ragged tuft | small ragged stromal fragments – "tufts" |
| short strip | columnar cells in short strips/palisading arrays (<6 cells) |
| sing col | single columnar cells |
| small ball | small rounded, balled up, isolated tissue fragments |
| small EH | small tissue fragments and sheets with myoepithelial cells |

## List of Abbreviations for the Cytological Criteria (continued)

| | |
|---|---|
| small nucleo | single and small nucleoli |
| small TF | small tissue fragments and scattered large tissue fragments with bare bipolar nuclei or some dispersed cells |
| stellate | branched, stellate stromal fragments with small epithelial tissue fragments attached |
| tubular | tubular structure |

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## Abstract

Cytological features of the various proliferative breast lesions have been described by numerous authors. The aim of this study was to evaluate the usefulness of these criteria in diagnosing epithelial hyperplasia with atypia (EHA), papillary lesions (PLs) and radial scar/complex sclerosing lesions (RS/CSLs) by fine needle aspiration biopsy (FNAB). EHA is a cytological diagnosis that raises a histological differential diagnosis of florid epithelial hyperplasia, atypical ductal hypeplasia and low-grade ductal carcinoma *in situ*. Papillary lesions in this study refer to intraduct papillomas of varying types including complex intraduct papillary lesions (CIPLs).

This study comprised both retrospective and prospective components. In the retrospective component, 77 cases found to be suitable for the study, were reviewed. They comprised 13 cases of EHA, 52 cases of PLs and 12 cases of RS/CSL. Cytological criteria were extracted from the literature, together with in-house criteria, which have been developed and used at the St. Vincent's Hospital, Sydney. Slides were reviewed and scored against these criteria. The results were analysed statistically to test if there was a significant association between the cytological criteria and the histological outcomes.

As the number of cases for the groups of EHA and RS/CSL were small compared to PLs, they were grouped together in the statistical analysis. One of the most significant findings was that the presence of stellate or meshwork stromal fragments is highly predictive of a PL. Papillary fragments were found infrequently and were of limited use in making the diagnosis of a PL, which is in contradiction to much of the literature.

The prospective part of the study aimed to test the sensitivity, specificity and positive predictive value of the criteria evaluated in the retrospective study in the diagnosis of PLs. Of the 1154 cases collected, 74 were suitable for slide review and scoring.

It was again found that meshwork stromal fragments occurred most frequently in PLs followed by stellate stromal fragments, whereas papillary fragments had the lowest

occurrence. However, all of these three criteria were found to be highly specific for PLs. The co-existence of either a proteinaceous background with macrophages and siderophages, or moderate to marked apocrine sheets further increased their specificities and positive predictive values.